

<b>Notice of Allowability</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/031,005	NELSESTUEN, GARY L.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Holly Schnizer	1656	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--**

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☐ This communication is responsive to the amendment filed 2/6/06.
2. ☒ The allowed claim(s) is/are 76,78,80,81 and 85-102.
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) ☐ All    b) ☐ Some\*    c) ☐ None    of the:
  1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\* Certified copies not received: \_\_\_\_\_.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

**THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS ( as "replacement sheets") must be submitted.
  - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review ( PTO-948) attached
    - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date \_\_\_\_\_.
  - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date \_\_\_\_\_.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

**Attachment(s)**

- |   |  |
|---|--|
| 1. <input type="checkbox"/> Notice of References Cited (PTO-892)  | 5. <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)            |
| 2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                | 6. <input type="checkbox"/> Interview Summary (PTO-413),<br>Paper No./Mail Date _____. |
| 3. <input type="checkbox"/> Information Disclosure Statements (PTO-1449 or PTO/SB/08),<br>Paper No./Mail Date _____ | 7. <input checked="" type="checkbox"/> Examiner's Amendment/Comment                    |
| 4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit<br>of Biological Material          | 8. <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance   |
|   | 9. <input type="checkbox"/> Other _____.   |

**PROPOSED**

**EXAMINER'S AMENDMENT**

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Elizabeth Kaytor on April 26, 2006.

The application has been amended as follows:

IN THE CLAIMS:

Please cancel claims 82, 103, 106-114, and 116

76. (Amended) A Factor VII or Factor VIIa polypeptide comprising a modified GLA domain that enhances membrane binding affinity of said polypeptide relative to a corresponding native Factor VII or Factor VIIa polypeptide, said modified GLA domain comprising at least one amino acid substitution selected from the group consisting of a) substitution of a hydrophobic amino acid residue at position 33, and b) substitution of a hydrophobic amino acid residue or ~~an aspartic acid or a~~ glutamic acid residue at position 34, wherein amino acid positions of the Factor VII or Factor VIIa polypeptide are numbered according to SEQ ID NO:3.

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81. (Amended) The polypeptide of claim 76, wherein ~~an aspartic acid or a~~ glutamic acid residue is substituted at position 34.

96. (Amended) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and an amount of Factor VII or Factor VIIa polypeptide effective to increase clot formation, wherein said Factor VII or Factor VIIa polypeptide comprises a modified GLA domain that enhances membrane binding affinity of said polypeptide relative to a corresponding native Factor VII or Factor VIIa polypeptide, said modified GLA domain comprising at least one amino acid substitution selected from the group consisting of a) substitution of a hydrophobic amino acid residue at position 33, and b) substitution of a hydrophobic amino acid residue or ~~an aspartic acid or a~~ glutamic acid residue at position 34, wherein amino acid positions of the Factor VII or Factor VIIa polypeptide are numbered according to SEQ ID NO:3.

98. (Amended) [A] An isolated mammalian host cell that expresses a Factor VII or Factor VIIa polypeptide, said Factor VII or Factor VIIa polypeptide comprising a modified GLA domain that enhances membrane binding affinity of said polypeptide relative to a corresponding native Factor VII or Factor VIIa polypeptide, said modified GLA domain comprising at least one amino acid substitution selected from the group consisting of a) substitution of a hydrophobic amino acid residue at position 33, and b) substitution of a hydrophobic amino acid residue or ~~an aspartic acid or a~~ glutamic acid residue at position 34, wherein amino acid positions of the Factor VII or Factor VIIa polypeptide are numbered according to SEQ ID NO:3.

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99. (Amended) A method of increasing clot formation in a mammal comprising administering an amount of a Factor VII or Factor VIIa polypeptide effective to increase clot formation in said mammal, wherein said Factor VII or Factor VIIa polypeptide comprises a modified GLA domain that enhances membrane binding affinity of said polypeptide relative to a corresponding native Factor VII or Factor VIIa polypeptide, said modified GLA domain comprising at least one amino acid substitution selected from the group consisting of a) substitution of a hydrophobic amino acid residue at position 33, and b) substitution of a hydrophobic amino acid residue or ~~an aspartic acid~~ or a glutamic acid residue at position 34, wherein amino acid positions of the Factor VII or Factor VIIa polypeptide are numbered according to SEQ ID NO:3.

102. (Amended) A method for producing a Factor VII or Factor VIIa polypeptide having a modified GLA domain comprising at least one amino acid substitution selected from the group consisting of a) substitution of a hydrophobic amino acid residue at position 33, and b) substitution of a hydrophobic amino acid residue or ~~an aspartic acid~~ or a glutamic acid residue at position 34, wherein amino acid positions of the Factor VII or Factor VIIa polypeptide are numbered according to SEQ ID NO:3, the method comprising (a) providing a culture of the mammalian host cell of claim 98 under conditions which permit expression of the polypeptide, and (b) recovering the polypeptide.

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The following is an examiner's statement of reasons for allowance:

The Amendment filed 2/6/06 overcomes the prior art rejections over Cheung et al. and Persson et al. The amendment also overcomes the double patenting rejection over 6,017,882 because the patent does not teach or suggest substituting a hydrophobic amino acid at position 33 or making a substitution at position 34 of SEQ ID NO:3. (The examiner notes that positions 33 and 34 are as referred to as positions 34 and 35 in the patent. The numbering used in the patent is based on factor IX which has an additional amino acid at position 4 relative to factor VII of SEQ ID NO: 3 (see Col. 5, lines 37-44)). The closest prior art of record to the present claims is considered to be McDonald et al. (Biochemistry (1997) 36: 5120-5127; ref. AQQ in IDS filed 6/7/02) which teaches that positions 33 and 34 (according to the numbering of SEQ ID NO:3) are important to membrane binding. However, McDonald et al. teaches that an aspartate at position 33 (referred to as position 34 in the McDonald et al. reference) corresponds with higher membrane binding affinity and that proteins containing an aspartate at position 33 show increased membrane binding capacity (p. 5126, Col. 1, 2<sup>nd</sup> full paragraph). Thus, McDonald et al. is considered to teach away from substituting a hydrophobic amino acid at position 33. In addition, while the alignment of the vitamin K dependent proteins on page 5125 of McDonald et al. shows that position 34 (position 35 in McDonald et al.) is important in membrane binding, McDonald et al. does not discuss making substitutions at this position and does not teach or suggest substitutions to hydrophobic amino acids or glutamic acid at position 34. Thus, the claims appear to be free of the prior art of record.

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Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

### Conclusions

Claims 76, 78, 80-81, and 85-102 are in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Holly Schnizer whose telephone number is (571) 272-0958. The examiner can normally be reached on Tuesday-Thursday from 10 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on (571) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Holly Schnizer  
April 27, 2006



NASHAAT T. NASHED PHD.  
PRIMARY EXAMINER